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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/496,444	02/02/2000	Yumin Tao	1109	6243

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EXAMINER
COLLINS, CYNTHIA E

ART UNIT	PAPER NUMBER
1638	28

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/496,444	TAO ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-18,22-25,27-53 and 64-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *22,65,70 and 75* is/are allowed.

6)☒ Claim(s) *2-18,23-25,27-53,64,66-69 and 71-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Appeal Brief filed March 25, 2003, paper no. 27, has been entered.

The finality of the Office action mailed September 20, 2002, is hereby withdrawn.

Claims 2-18, 22-25, 27-53, 64-69, 70-75 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claims 2-18, 23-25, 27-53, 64, 66-69 and 71-74 are rejected under 35 U.S.C. 112, first paragraph, for written description, for the reasons of record set forth in the office action mailed September 20, 2002.

Applicant's arguments filed March 25, 2003, have been fully considered but they are not persuasive.

Applicant argues that the rejected claims meet the written description requirement because they provide the necessary structural features in requiring that the polynucleotides have at least 80% identity to SEQ ID NO:1. Applicant argues that in requiring that the polynucleotides have at least 80% identity to SEQ ID NO:1, the claims recite structural features common to members of the genus which constitute a substantial portion of the genus. Applicant argues that the rejected claims meet the written description requirement because they also provide the necessary functional features in requiring that the polynucleotide be capable of modulating the level of cyclin E protein in a cell (brief page 5).

The Examiner maintains that merely reciting that the polynucleotides have at least 80% identity to SEQ ID NO:1 does not describe the structural features common to polynucleotides having at least 80% identity to SEQ ID NO:1 that are capable of modulating the level of cyclin E protein in a cell. Similarly, the Examiner maintains that merely reciting that the polynucleotides be capable of modulating the level of cyclin E protein in a cell does not describe those polynucleotides having at least 80% identity to SEQ ID NO:1 that are capable of modulating the level of cyclin E protein in a cell.

Applicant additionally points to Example 9 of the Synopsis of Application of the Written Description Guidelines in which a claim to an isolated nucleic acid that hybridizes under highly stringent conditions to a sequence is considered adequately described, even though only one sequence is disclosed, and Applicant points out that percent sequence identity correlates strongly with hybridization (brief pages 5-6).

Example 9 of the USPTO Written Description Guidelines states that the specification in question discloses a single cDNA of SEQ ID NO:1 "which encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity", that the specification includes an example wherein the complement of SEQ ID NO:1 was used under highly stringent hybridization conditions for the isolation of nucleic acids "that encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity", and that although the hybridizing nucleic acids were not sequenced, they were expressed and "several were shown to encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity". In contrast, the instant specification discloses a single polynucleotide of SEQ ID NO:1 that complements G1

cyclin deficient yeast. The instant specification does not disclose any other novel polynucleotide, obtained by hybridization or having at least 80% sequence identity to SEQ ID NO:1, that also complements G1 cyclin deficient yeast. Accordingly, in the instant case, the disclosure of a single polynucleotide of SEQ ID NO:1 that complements G1 cyclin deficient yeast does not support the description of polynucleotides having at least 80% sequence identity to SEQ ID NO:1 that are capable of modulating the level of cyclin E protein in a cell.

Applicant also points to the written description guidelines as providing that there may be situations where one species adequately supports a genus. Applicant argues that what constitutes a representative number of species depends on whether one of skill in the art would recognize that Applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Applicant points to the specification as disclosing a definition of a cyclin E polynucleotide as encoding a polypeptide that binds to Cdk2 and Rb proteins, contains a cyclin box, and contains a conserved TTPXS motif near the carboxy-terminus (pages 6-7).

The Examiner maintains that the instant situation is not one in which the disclosure of a one species adequately supports the description of a genus. While the specification discloses that a cyclin E polynucleotide is defined as encoding a polypeptide that binds to Cdk2 and Rb proteins, as containing a cyclin box, and as containing the conserved TTPXS motif near the carboxy-terminus, the specification does not disclose whether nucleic acid sequences having at least 80% identity to SEQ ID NO:1 and having these characteristics would also be capable of modulating the level of cyclin E protein in a cell. Since the specification discloses only one

functional sequence encompassed by the claimed genus, and since a correlation between the structural and functional characteristics of the polypeptide encoded by polynucleotides of the claimed genus is not disclosed and does not appear to be known, the disclosure of one functional species in the instant case does not adequately support the description of the claimed genus.

Applicant also argues that polynucleotides requiring 80% identity to SEQ ID NO:1 do not read on widely variant species, and therefore do not require a laundry list of potential sequences (brief page 7).

The Examiner disagrees that polynucleotides requiring 80% identity to SEQ ID NO:1 do not read on widely variant species. The sequence listing indicates that SEQ ID NO:1 is a polynucleotide consisting of 1636 base pairs. Accordingly, any polynucleotide consisting of 1636 base pairs that lacks any unspecified 327 base pairs of SEQ ID NO:1 would be encompassed by the claim. Since a change in even a single nucleotide has the potential to alter the amino acid sequence of a polypeptide encoded by a polynucleotide, the Examiner maintains that polynucleotides requiring 80% identity to SEQ ID NO:1 do read on widely variant species.

Applicant additionally points to the disclosure in the specification of specific methods, well known in the art, for obtaining acceptable variant sequences, and argues that the disclosure of additional sequences would be of negligible value for determining how to vary SEQ ID NO:1 in order to obtain functional variants. Applicant further argues that obtaining the claimed products and practicing the claimed methods is within the abilities of one skilled in the art, especially in view of the methods disclosed in the specification (brief pages 7-11).

The Examiner maintains that the disclosure in the specification of specific methods for obtaining acceptable variant sequences does not describe the structural features common to polynucleotides having at least 80% identity to SEQ ID NO:1 that are capable of modulating the level of cyclin E protein in a cell. The Examiner further maintains that the disclosure of additional sequences would be of value for determining how to vary SEQ ID NO:1 in order to obtain functional variants, as the disclosure of additional functional sequences provides information regarding which nucleotides of SEQ ID NO:1 would be retained in a functional variant having 80% sequence identity to SEQ ID NO:1. It does not necessarily follow that one will obtain the claimed variant sequences because practicing the claimed methods is within the abilities of one skilled in the art, as the specification does not describe any functional variant having at least 80% identity to SEQ ID NO:1 that is capable of modulating the level of cyclin E protein in a cell.

The Examiner maintains that an adequate written description of a claimed genus requires a description of both a structure and a function that is correlated with it. While claim 64 recites a specific percent identity (80%) of a specific nucleic acid sequence (SEQ ID NO:1), a specific function correlated with a plant cyclin E polynucleotide having at least 80% identity to SEQ ID NO:1 is not recited. Furthermore, while the specification does disclose that a cyclin E polynucleotide is defined as encoding a polypeptide that binds to cdk2 and Rb proteins, as containing a cyclin box, and as containing the conserved TTPXS motif near the carboxy-terminus, the specification does not disclose whether nucleic acid sequences having at least 80% identity to SEQ ID NO:1 and having the structural elements of a cyclin box and a conserved

TTPXS motif near the carboxy-terminus would encode cyclin E proteins that could be used to practice the claimed invention. The Examiner does not dispute that the isolated nucleic acid of SEQ ID NO:1 has the structural and functional characteristics of a nucleic acid encoding a functional cyclin E protein, but the rejected claims are not limited the isolated nucleic acid of SEQ ID NO:1, or to isolated nucleic acids encoding a functional cyclin E protein.

Claims 2-18, 23-25, 27-53, 64, 66-69 and 71-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid of SEQ ID NO:1 or an isolated nucleic acid encoding SEQ ID NO:2, and complementary nucleotides thereof, does not reasonably provide enablement for polynucleotides having at least 80% identity to the entire coding region of SEQ ID NO:1 and complementary nucleotides thereof, or for transgenic plants comprising said polynucleotides, or for methods of using said polynucleotides to achieve specific phenotypic effects in transgenic plant cells or plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the office action mailed September 20, 2002, and for the reasons set forth below.

Applicant's arguments filed March 25, 2003, have been fully considered but they are not persuasive.

Applicant argues that the specification provides guidance on sequence modifications and variants, as well as methods to identity such compositions. Applicant argues that the testing required to determine the functionality of the claimed sequences is therefore routine. Applicant

points to the factors set forth in *In re Wands* for the determining whether the experimentation required to practice an invention would be undue, and points out that the court in Wands placed emphasis on the amount of experimentation required to practice any particular member of the genus, rather than the amount of experimentation required to practice the entire genus (brief pages 12-13). Applicant argues that the claimed sequences could easily be tested for activity using the methods outlined in the specification, and that such testing would not constitute undue experimentation, as such testing is within the abilities of one skilled in the art. Applicant argues that because the testing required to identity the claimed sequences is routine, additional specific sequences need not be provided to enable sequences having at least 80% identity to SEQ ID NO:1 (brief page 14).

The Examiner maintains that the specification does not disclose modifications or variants of SEQ ID NO:1. The Examiner also maintains that the disclosure of methods to identify compositions and assays to determine their functionality does not provide sufficient guidance for one skilled in the art to determine, without undue experimentation, which isolated nucleic acids encode a protein that could be used to practice the claimed invention, as the undue experimentation does not lies in using the disclosed methods to identify compositions and assays to determine their functionality. The undue experimentation lies in the process of selecting from among the numerous claimed polynucleotides those polynucleotides that would be likely to modulate the level of cyclin E protein or produce the effects recited in the claims, prior to confirming their functionality. Absent guidance for discriminating between functional and nonfunctional embodiments prior to confirming functionality, the amount of experimentation

required to practice any particular member of the genus other than SEQ ID NO:1 or sequences encoding SEQ ID NO:2 is undue.

Applicant further points to the multitude of chemical patents that have issued with generic claims reading on tens to hundreds of thousands of individual members. Applicant also points to patents that have issued the chemical and pharmacological disciplines containing open-ended R groups that result in innumerable possible structures, and argues that the present specification and claims provide at least as much direction as to the structure of the claimed nucleic acid. Applicant points out that the court in *Amgen* stated that DNA was a chemical compound, and that in light of such a statement the application of chemical and pharmacological case law is appropriate to cases involving the patentability of DNA sequences (reply pages 14-15).

The Examiner is not in a position to comment on the prosecution in other applications, and each application is examined on its own merits. Patents are not properly precedent, and it is impossible to be privy to the prosecution history of all of the patents issued. While the Examiner does not dispute that a multitude of chemical patents have issued generic claims reading on tens of hundreds to thousand of individual members, and that many patents containing open-ended R groups are issued in the chemical and pharmacological disciplines, the relevancy of this observation to the instant situation is unclear, as the patents referred to are undoubtedly directed to a multitude of different kinds of chemical compounds having different properties and uses. There is no per se rule regarding the patentability of chemical compositions containing open-ended R groups, and the potential effect of an open-ended R group on the function of the

resultant compound as a whole would have to be considered in order to determine the patentability of any chemical composition containing open-ended R groups.

With respect to the application of chemical and pharmacological case law to the patentability of the instant invention, any particular case cited by Applicant as being relevant to the enablement of the instant invention (polynucleotides encoding proteins) will be considered. With respect to the specifically cited case of *Amgen*, presumably *Amgen v. Chugai*, 927 F.2d 1200, the Examiner maintains that the cited case does not support the enablement of sequences having at least 80% identity to SEQ ID NO:1 on the basis of the disclosure of a single polynucleotide sequence of SEQ ID NO:1. In *Amgen*, claims directed to all possible DNA sequences encoding any polypeptide having an amino acid sequence sufficiently duplicative of EPO to possess the property of increasing the production of red blood cells were found to lack enablement because the disclosure of only a few functional analog sequences did not provide sufficient guidance to enable the full scope of the generic claim. Here, the disclosure of a single functional polynucleotide sequence of SEQ ID NO:1 does not support the enablement of sequences having at least 80% identity to SEQ ID NO:1 because the specification does not provide sufficient guidance for discriminating between operative and inoperative embodiments that fall within the scope of the claim.

Guidance for making and using the claimed invention is also necessary for enablement because it is unpredictable whether expression of the claimed polynucleotides in plant cells or plants would result in any of the claimed effects on cell division, cell growth, crop yield, organ growth, etc. The claimed effects are unpredictable because the prior art teaches that progression

through the cell cycle, including the G1 to S transition, is affected by the activity of numerous proteins in addition to cyclin E. Furthermore, cyclin E itself does not function independently. For example, Reed (Cancer Surv. 1997, Vol. 29, pages 7-23) teaches that cyclin E functions by association with a single catalytic partner, CDK2 (page 9 third paragraph). Reed also teaches that while cyclin E appears to be essential for entry into the S phase of the cell cycle, cyclin E does not appear to be rate-limiting for the G1/S phase transition (page 10 first paragraph). Furthermore, the activity of the cyclin E/CDK2 complex itself is subject to regulation by additional proteins. Both CDK inhibitory proteins and negative phosphorylation can affect the activity of cyclinE/CDK2. For example, Reed teaches that The Cip/Kip family of cyclin-dependent kinase inhibitor proteins are active against the cyclin E/CDK2 complex (page 12 third paragraph), and that CDK2 can also be inhibited by phosphorylation on Tyr-15 and possibly Thr-14 (page 14 last paragraph). Furthermore, although it has been suggested that cyclin E contributes to RB phosphorylation, Reed teaches that there is little consensus on the critical substrates for cyclin E/CDK2, and that experimental evidence suggests the existence of alternative unidentified targets for cyclin E/CDK2 activity (page 16 last paragraph). It is unpredictable whether the various proteins that positively and negatively influence cyclin E function would be present in plant cells at the appropriate time, in the appropriate place, and in the appropriate quantity such that expressing the claimed polynucleotides would result in the desired phenotypic effects.

The claimed effects are also unpredictable because the prior art teaches that the effect of overexpressing cyclin E in cells is unpredictable. For example, Sgambato et al. teach that overexpression of the same cyclin E cDNA in different cell types produces different biological

effects (Cancer Research, 1996, Vol. 56, pages 1389-1399). Sgambato et al. teach that expression of a human cyclin E cDNA HU4 in HC11 mouse mammary epithelial cells was associated with an increase in cell size, a lengthening of the G1 phase of the cell cycle, and inhibition of both anchorage-dependent and -independent growth, in contrast to previously reported results in which overexpression of the same cDNA in rat and human fibroblasts was associated with a decrease in cell size, a shortening of the G1 phase of the cell cycle, and a stimulation of cell growth (page 1389 abstract and column 2 last paragraph; page 1393 Tables 1 and 2; page 1397 column 2 second paragraph). Sgambato et al. attributed the effects observed in HC11 mouse mammary epithelial cells to increased expression of the cyclin-dependent kinase inhibitor $p27^{Kip1}$ in cyclin E overexpressing cells (page 1395 Figure 5; page 1397 column 2 last paragraph). The effect of expressing the claimed polynucleotides in plant cells would also be unpredictable, since plants as well as animals are composed of different cell and tissue types.

In view of the teachings of the prior art that that progression through the cell cycle is affected by the activity of numerous proteins in addition to cyclin E, the requirement for the presence of CDK2 and cyclin E/CDK2 substrates to effect cyclin E function, the susceptibility of the cyclin E/CDK2 complex to the inhibitory effects of other proteins, and the unpredictability of the effects of overexpressing cyclin E in different cell types, and in view of the lack of guidance provided by the specification, it would require undue experimentation for one skilled in the art to achieve the effects recited in the claims by expressing the claimed polynucleotides in transgenic plant cells or plants.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23, 27-33, 35-37, 39-64 and 71, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23, 39-41, 44-64 and 71 are indefinite in the recitation of "modulating", "modulate" or "modulated" . The terms "modulating", "modulate" or "modulated" are relative terms, as they imply a gradual adjustment for keeping a process in proper measure or proportion, for which there is no comparative basis.

Claim 23 is indefinite in the recitation of "time sufficient to induce expression of the polynucleotide sufficient to modulate CycE protein in the cell". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how long plant cells must be grown under cell-growing conditions in order to modulate CycE protein in the cell.

Claims 27, 30, 36, 46, 47 and 51 are indefinite in the recitation of "alter", as "alter" is a relative term that lacks a comparative basis. It is unclear what the alteration is relative to. For example, is the increase relative to a nontranformed plant cell grown under the same conditions? It is also unclear in what way cell division, cell growth, plant height, plant size, the percent time of arrest, the amount of time in a cycle, and lag time are altered, as each of these characteristics may be altered in more than one way. For example, is the rate of cell division increased? Is the rate of cell division decreased? Is cell division arrested? Does the cell grow larger? Does the cell grow smaller? Is the plant taller? Is the plant shorter? Is the plant wider? Is the plant more narrow? Is the percent time of arrest longer? Is the percent time of arrest shorter? Is the amount

of time in a cycle longer? Is the amount of time in a cycle shorter? Is the lag time longer? Is the lag time shorter?

Claim 27 is indefinite in the recitation of "an amount sufficient to alter cell division". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to alter plant cell division.

Claims 28, 32, 35, 43, 45, 49, 50 and 53 are indefinite in the recitation of "increase", as "increase" is a relative term that lacks a comparative basis. It is unclear what the increase is relative to. For example, is the increase relative to a nontranformed plant cell grown under the same conditions?

Claim 28 is indefinite in the recitation of "an amount sufficient to increase the number of dividing cells". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to increase the number of dividing cells.

Claim 28 is indefinite in the recitation of "cells". There is insufficient antecedent basis for "cells" in claim 23 from which claim 28 depends.

Claims 29 and 48 are indefinite in the recitation of "improve", as "improve" is a relative term that lacks a comparative basis. For example, are the transformation frequencies and cell responses improved relative to a nontranformed plant cell grown under the same conditions?

Claim 29 is indefinite in the recitation of "an amount sufficient to improve transformation frequencies". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to improve transformation frequencies.

Claim 30 is indefinite in the recitation of "an amount sufficient to alter cell growth". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to alter cell growth.

Claim 31 is indefinite in the recitation of "positive growth advantage". It is unclear what type of growth advantage the cell exhibits, and it is unclear what the advantage is relative to. For example, does the cell grow bigger? Faster? Both? Is the growth advantage relative to a nontranformed plant cell grown under the same conditions?

Claim 31 is indefinite in the recitation of "an amount sufficient to provide a positive growth advantage". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to provide a positive growth advantage.

Claim 32 is indefinite in the recitation of "an amount sufficient to increase the growth rate". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to increase the growth rate.

Claim 33 is indefinite in the recitation of "wherein the cell is a plant cell". The phrase "wherein the cell is a plant cell" does not appear to further limit the claimed invention, as the method of claim 23 requires transforming and growing a plant cell.

Claim 33 is indefinite in the recitation of "capable of expressing CycE protein". It is unclear what the claim is meant to encompass, as any regenerated plant would inherently possess the capability of expressing a CycE protein.

Claim 35 is indefinite in the recitation of "an amount sufficient to increase crop yield". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to increase crop yield.

Claim 36 is indefinite in the recitation of "an amount sufficient to alter plant height or size". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to alter plant height or size.

Claims 37 and 42 are indefinite in the recitation of "enhance", as "enhance is a relative term that lacks a comparative basis. It is also unclear what type of enhancement is intended, as organ growth and embryogenic response may undergo more than one type of enhancement. For example, organ growth could be enhanced by an increase in the size of an organ, or an increase in the number of organs per plant. An embryogenic response could be enhanced by an increase in the rate of response, or an increase in the number of responses.

Claim 37 is indefinite in the recitation of "inhibit", as inhibit is a relative term that lacks a comparative basis. Is organ growth inhibited relative to a nontranformed plant cell grown under the same conditions?

Claim 37 is indefinite in the recitation of "an amount sufficient to enhance or inhibit organ growth". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to enhance or inhibit organ growth.

Claim 42 is indefinite in the recitation of "embryogenic response". It is unclear what type of embryogenic response the claim encompasses, as embryogenesis may respond differentially to the presence or absence of a variety of factors, such as hormones, temperature, light, etc.

Claim 42 is indefinite in the recitation of "an amount sufficient to enhance embryogenic response". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to enhance embryogenic response.

Claim 43 is indefinite in the recitation of "an amount sufficient to increase callus induction". The metes and bounds of the phrase are unclear, as neither the specification nor the prior art teaches how much CycE protein must be present to increase callus induction.

Claim 48 is indefinite in the recitation of "the response of cells to environmental stress". It is unclear what type of environmental stress response the claim encompasses, as cells may respond differently to the presence or absence of a variety of environmental stresses, such as by dying, or by synthesizing a variety of different compounds (such as heat shock proteins, compatable solutes, antioxidants, etc.) that specifically protect the cell against a variety of different stresses such as heat, cold, dehydration, and oxidative stresses.

Claim Rejections - 35 USC § 101 and 35 USC § 112

Claims 16-18 are rejected under 35 U.S.C. 101 as not being supported by a specific and substantial utility, for the reasons of record set forth in the office action mailed September 20, 2002.

Applicant's arguments filed March 25, 2003, have been fully considered but they are not persuasive.

Applicant argues that there is clear evidence in the literature that overexpression of cyclin E produces altered effects on transformed cells. Applicant points to page 9 of the specification which indicates that cyclin E genes from heterologous species have previously been found to

complement *Saccharaomyces cervesisiae* cells lacking G1 cyclin function, and that cyclin E overexpression has previously been found to stimulate the S-phase of the cell cycle in various cell types in both *Drosophila* and mammalian cells, and that evidence across a variety of fauna suggests that cyclin E promotes cell cycle entry into the S-phase, and is involved in such processes as endocycling and organ pattern formation. Applicant additionally points to WO 00/17364, which discloses that increased transformation results from transformation of plant cells with cyclin D (brief, pages 15-16).

The Examiner does not dispute the teachings of the prior art with respect to the effect of expressing E-type cyclins in animal and yeast cells, but maintains that Applicants have not demonstrated, and the prior art does not teach, a specific and substantial utility for plants or plant cells that express a polynucleotide of SEQ ID NO:1, or for plants or plant cells that express a polynucleotide encoding an E-type cyclin. With respect to the utility of expressing polynucleotides encoding D-type cyclins in plant cells, the Examiner maintains that the utility of expressing an E-type cyclin in plant cells cannot be predicted on the basis of the utility of expressing polynucleotides encoding D-type cyclins in plant cells, as the prior art teaches that D-type cyclins and E-type cyclins are different classes of cyclins that exhibit structural and functional differences as well as similarities, such that their interchangeability cannot be presumed. For example, Reed (Cancer Surv. 1997, Vol. 29, pages 7-23) teaches that D-type cyclins associate with and activate the cyclin-dependent kinases CDK4 and CDK 6, which are not histone H1 kinases and which are structurally different from prototypical yeast CDKs, whereas E-type cyclins associate with and activate the cyclin-dependent kinase CDK2, which is a histone H1 kinase and which is structurally similar to prototypical yeast CDKs (page 9 second

and third paragraphs). Furthermore, although the RB protein appears to be a substrate for both D-type and E-type cyclin/CDK complexes, Reed teaches that experiments suggest the presence of additional critical substrates for cyclin E/CDK2 in the cell (page 16 second paragraph).

Claims 16-18 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Remarks

Claims 22, 65, 70 and 75 are allowed.

Claims 2-18, 23-25, 27-53, 64, 66-69 and 71-74 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
July 13, 2003

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600